

## PATENT COOPERATION TREATY

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## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 17 February 1998 (17.02.98)	
<b>International application No.</b> PCT/US97/10486	<b>Applicant's or agent's file reference</b>
<b>International filing date</b> (day/month/year) 17 June 1997 (17.06.97)	<b>Priority date</b> (day/month/year) 17 June 1996 (17.06.96)
<b>Applicant</b> TSICHLIS, Philip et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

12 January 1998 (12.01.98)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer

N. Lindner

Facsimile No. (41-22) 740 14 35

Telephone No. (41-22) 348 83 38

Copy for the receiving Office (RO/US)  
PATENT COOPERATION TREATY

09 202549 PCT/US97/10486

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NOTIFICATION OF THE RECORDING  
OF A CHANGE

(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

REED, Janet, E.  
Dann, Dorfman, Herrell & Skillman  
Suite 720  
1601 Market Street  
Philadelphia, PA 19103  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 28 November 1997 (28.11.97)	
Applicant's or agent's file reference	IMPORTANT NOTIFICATION
International application No. PCT/US97/10486	International filing date (day/month/year) 17 June 1997 (17.06.97)

1. The following indications appeared on record concerning:

☒ the applicant ☒ the inventor ☐ the agent ☐ the common representative

Name and Address

ZWEIDLER-McKAY, Patrick  
310 South Easron Road #A214  
Glenside, PA 19038  
ETATS-UNIS D'AMERIQUE

State of Nationality

US

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address

ZWEIDLER-McKAY, Patrick  
2nd floor  
66 Cameron Avenue  
West Somerville, MA 02144-2404  
ETATS-UNIS D'AMERIQUE

State of Nationality

US

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☐ the elected Offices concerned  
☐ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

N. Lindner

Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

REC'D

13 OCT 1998

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference FCCC 96-11	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA 416)	
International application No. PCT/US97/10486	International filing date (day/month/year) 17 JUNE 1997	Priority date (day/month/year) 17 JUNE 1996
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant FOX CHASE CANCER CENTER		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets.
- ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  12 JANUARY 1998	Date of completion of this report  26 AUGUST 1998
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer  ROBERT SCHWARTZMAN
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US97/10486

## I. Basis of the report

1. This report has been drawn on the basis of *(Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments)*

- ☒ the international application as originally filed.
- ☒ the description, pages 1-33 , as originally filed.  
pages NONE , filed with the demand.  
pages NONE , filed with the letter of \_\_\_\_\_  
pages \_\_\_\_\_ , filed with the letter of \_\_\_\_\_
- ☒ the claims, Nos. 1-25 , as originally filed.  
Nos. NONE , as amended under Article 19.  
Nos. NONE , filed with the demand.  
Nos. NONE , filed with the letter of \_\_\_\_\_  
Nos. \_\_\_\_\_ , filed with the letter of \_\_\_\_\_
- ☒ the drawings, sheets/~~fig~~ 1-4 , as originally filed.  
sheets/~~fig~~ NONE , filed with the demand.  
sheets/~~fig~~ NONE , filed with the letter of \_\_\_\_\_  
sheets/~~fig~~ \_\_\_\_\_ , filed with the letter of \_\_\_\_\_

2. The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/~~fig~~ NONE

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US97/10486

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims	<u>1-25</u>	YES
	Claims	<u>NONE</u>	NO
Inventive Step (IS)	Claims	<u>1-25</u>	YES
	Claims	<u>NONE</u>	NO
Industrial Applicability (IA)	Claims	<u>1-25</u>	YES
	Claims	<u>NONE</u>	NO

**2. CITATIONS AND EXPLANATIONS**

Claims 1-25 meet the criteria set out in PCT Article 33(2)-(4) because the prior art does not teach or fairly suggest mutated binding sites for the transcriptional repressor Gfi-1.

----- NEW CITATIONS -----  
NONE

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The description is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 5 because it fails to adequately enable practice of the claimed invention because:

Claim 25 is drawn to a method of treating a pathological condition related to expression of an aberrant gene by administering to the patient an expression vector comprising a non-aberrant counterpart to the aberrant gene linked to a promoter a mutated binding site for the transcriptional repressor Gfi-1. The claim is extremely broad, encompassing any disease, any gene any expression vector and any method of administration. The claimed invention, a method of treating a disease by administering recombinant DNA, known as gene therapy, is highly unpredictable. Despite years of intense research and many clinical trials there has yet to be any definitive example of the successful treatment of a disease using a gene therapy protocol. The main obstacles to effective therapy are the efficient delivery of the therapeutic gene to the appropriate target cells and the sustained expression of the gene. At the time the present invention was made, no predictable method for effective gene therapy had been developed. Thus, the skilled artisan would have to rely on the present description to teach how to carry out the claimed method. However, the description is completely silent regarding methods for gene therapy. Therefore, the description fails to adequately enable the claimed invention.

Claim 25 is objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US97/19486

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

~~Sheet 10~~

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(6): C07H 21/04; C12N 15/09, 15/79; A61K 31/70 and US Cl.: 536/23.52, 24.1; 435/172.3, 320.1; 514/44

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Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
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DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						



# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US97/10486

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) C07H 21/04; C12N 15/09, 15/79; A61K 31/70  
US CL 536/23.52, 24.1; 435/172.3, 320.1; 514/44

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.52, 24.1; 435/172.3, 320.1, 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN:Medline, Biosis, Embase, CAPUS, WPIDS, JAPIO, PATOSEP, PATOSWO; APS

Search Terms: GFI-1, growth factor independence, transcription

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P --- Y,P	ZWFIDLER-MCKAY et al. Gfi-1 encodes a nuclear zinc finger protein that binds DNA and functions as a transcriptional repressor. Molecular and Cellular Biology. August 1996, Vol. 16, No. 8, pages 4024-4034, see entire document.	1-10, 12-19, 21-24 ----- 11, 20
X,P --- Y,P	GRIMES et al. The Gfi-1 proto-oncoprotein contains a novel transcriptional repressor domain, SNAG, and inhibits G1 arrest induced by interleukin-2 withdrawal. Molecular and Cellular Biology. November 1996, Vol. 16, No. 11, pages 6263-6272, see entire document.	1, 7-10, 12, 13, 21-24 ----- 2-6, 11, 14-20

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
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"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

02 SEPTEMBER 1997

Date of mailing of the international search report

09 OCT 1997

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# INTERNATIONAL SEARCH REPORT

International application No  
PCT/US97/10486

C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GILKS et al. Prolactin (PRL)-dependent expression of a zinc finger protein-encoding gene, Gfi-1, in Nb2 lymphoma cells: constitutive expression in autonomous sublines. Endocrinology. 1995, Vol. 136, No. 4, pages 1805-1808, see entire document.	1-25
A	GILKS et al. Progression of interleukin-2 (IL-2)-dependent rat T cell lymphoma lines to IL-2-independent growth following activation of a gene (Gfi-1) encoding a novel zinc finger protein. Molecular and Cellular Biology. March 1993, Vol. 13, No. 3, pages 1759-1768, see entire document.	1-25